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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,470	07/21/2003	Debbi Drane	017227-0190	4517
22428	7590	09/02/2008	EXAMINER	
FOLEY AND LARDNER LLP			LI, BAO Q	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/622,470	Applicant(s) DRANE ET AL.
	Examiner BAO LI	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 17 June 2008.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,44,45,49-66 and 70-99 is/are pending in the application.
 - 4a) Of the above claim(s) 56-62,77-83 and 86-99 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1, 44-45, 49-55, 63-66, 70-76, 84-85 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) Notice of Informal Patent Application
- 6) Other: _____

DETAILED ACTION

Response to Amendment

The amendment and response filed on May 13, 2008 have been acknowledged. Claims 1, 44-45, 50-51, 56-62, 64-66, 71-72, 77-83 have been amended. Claims 2-43, 46-48, 67-69 have been canceled. Claims 1, 44-45, 49-66, 70-99 are pending. Claims 56-62, 77-83 and 86-99 were withdrawn from consideration. Claims 1, 44-45, 49-55, 63-66, 70-76, 84-85 are considered before the examiner.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Claims 1, 44, 49-55, 64-66, 70-76 are still rejected under 35 U.S.C. 102(b) as being anticipated by Simmonds et al. (A) (WO 94/25602A1) or under 35 U.S.C. 102(e) as being anticipated by Simmonds et al. (B) (US Patent No. 6,881,821B2) or (C) (US 7,198,892B2) in light of the teaching by Sjolander et al. (Advanced Drug Delivery Reviews

Volume 34, Issues 2-3, December 1998, Pages 321-338.

3. In the response, Applicants still provide the argument that Simmonds et al. do not teach the attachment of *a positively charged antigen* to a negatively charged ISCOM. Applicants point out that the peptides disclosed by the reference in Example 3 are *negatively charged*. Therefore the negatively charged peptides could not be "electrostatically associated" with a negatively charged organic complex cited in the instant claims. Hence the reference simply cannot anticipate the present invention.

4. Applicants' argument has been fully considered; however, it is not found persuasive for the following reasons:

5. a). The reference does not only limit the peptides disclosed in example 3 suitable for attachment to the ISCOM. Simmonds et al. teach that any antigen of HCV antigen polypeptide or polyproteins can be expressed by a recombinant DNA technique, and any HCV antigen is suitable for attaching to ISCOM or liposome.

6. b). ISCOM in nature is a negative charged antigen carrier or adjuvant. Without any other chemical conjugation step by other chemical compound or linker, attaching to a negative charged carrier/adjuvant with a protein/peptide antigen is inherently via an electrostatic association. Simmonds et al. do not teach that any chemical conjugation method in any of the references cited. Therefore, the attachment of a HCV antigen to negatively charged ISCOM is inherently an interaction between the negatively charged ISCOM and positively charged HCV antigen. Otherwise, if the HCV antigen does not have opposite charge, the attachment would not occur.

7. c). The immunogenic composition taught by Simmonds's references (A to C) all comprises a HCV immunogene and a negatively charged ISCOM (See page 24 of A, column 10 in B and column 11 in C), wherein the ISCOM is the complex made by saponin, cholesterol and optionally a lipid, preferably lipid A in light of the teaching by Sjolander et al. Moreover, none of references by Simmonds et al. teach to use alum or oil-in water formulation. To this context, this immunogenic composition meets the limitation of claims 1, 44, 46-55, 64-76, and 86.

8. Because the immunogenic composition taught by Simmonds et al. comprises an HCV antigen, and an organic complex of ISCOM made by a saponin (QS21), cholestrosol, and a lipid, this is sufficient enough to meet the limitation cited in the rejected claims. When the reference teaches a product that appears to be the same as or an obvious variant of regardless how it is

made. The Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products unless the applicants provide the evidence that the claimed product is structurally and/or functionally different from the cited prior arts.

9. MPEP cites “[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer.” *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

10. For the reasons described above, the rejection is therefore, maintained.

11.

12. Claims 1, 44, 49, 50, 51, 54, 55, 64, 70-72, 75 and 76 are still rejected under 35 U.S.C. 102(b) as being anticipated by Garcon et al. (WO 96/33739A1).

13. Applicants traverse the rejection and submit that Garcon’s reference is broadly directed to vaccine compositions comprising an antigen, saponin and sterol, and in some embodiments of lipid, preferably MPL. Most of the disclosure and examples of Garcon relates to its “preferred compositions” which comprise liposomes. Applicants could find only one teaching on page 2 that the invention includes “compositions where the sterol/immunologically active saponin fraction forms an ISCOM structure. Notably, there is no express disclosure of how such an ISCOM would be formulated with the antigen. Pages 4-5 of Garcon cite references that describe methodologies that can be used in making its vaccines. Page 5 cites U.S. Patent 4,235,877 for encapsulation with liposomes, and cites U.S. Patent 4,372,945 and U.S. Patent 4,474,757 for “[c]onjugation of proteins to macromolecules.” Notably, the ‘945 and ‘757 patents disclose covalent conjugation methodologies. (Copies of these patents are attached hereto for the Examiner’s convenience).

14. Applicants’ argument has been fully considered; however, it is not accurate and persuasive. As it is admitted by Applicants that the immunogenic composition taught by Carcon et al. is the composition containing a saponin and a sterol that forms ISCOM, which is taught suitably for formulating any antigen including a HCV antigen. Moreover, Carcon et al. also teach that the antigen composition formulated with ISCOM (SQ21+Sterol (SUV)) can be further added

with MPL (QS21+SUV+MPL), such that the cytotoxic T cell activity is much higher than that comprising QS21 plus SUV or SQ21 alone. Because the saponin plus sterol form ISCOM, wherein the ISCOM is a negatively charged antigen carrier/adjuvant, this is sufficient enough to meet the limitation of the rejected claims.

15. Furthermore, in contrast to Applicants' assertion that Garcon's methodologies for the association between the antigen and ISOCM are related to encapsulation rather than electrostatically association, Carcon et al. describe on page 2 that "the antigen in the immunogenic complex can be contained within the vesicle membrane or **outside** the vesicle membrane. Preferably soluble antigens are **outside** and hydrophobic or lipidated antigen is either contained inside or outside the membrane. In the instant case, HCV antigens are all hydrophobic. Carcon et al. also disclose that the vaccine composition formulated by ISCOM or other liposome will not require any specific carrier and be formulated in an aqueous or other pharmaceutically acceptable buffer. Whereas the alum or an oil in water emulsion is only an option rather than an obligation (See page 2). Carcon et al. also teach that liposome is may be added into QS21/cholesterol mixture (ISCOM), which reduces the lytic activity of QS21 and increase the negative charge and stability of the complex of ISCOM (pages 6-8), wherein the liposome can be phospholipid, such as phospholipid A.

16. For these reasons described above, the association the attachment of a HCV antigen to negatively charged ISCOM is inherently an interaction between the negatively charged ISCOM and positively charged HCV antigen. Otherwise, if the HCV antigen does not have opposite charge, the attachment would not occur.

17. MPEP cites "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)

18. Therefore, the disclosure of the cited reference still meet the limitation of the claims, the rejection is maintained.

19.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

21. Claims 1, 44, 49-55, 63-66, 70-76 and 84-85 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Simmonds et al. (A) (WO 94/25602A1) or (B) or (C) as cited above in view of the teaching by Cerny et al. (J. Clin. Invest. 1995 Feb; 95(2):521-30).

22. In addition argue that the references by Simmonds et al. do not teach the positively charged antigens, Applicants further argue that Cerny et al. only teach that the HCV T cell epitopes, the combination of Cerny et al. with Simmond et al. still leave the skilled artisan with no guidance to form an immunogenic complex comprising a negative charged organic complex and a positively charged antigen.

23. Applicants' argument has been respectfully considered; however, it is not found persuasive because Simmonds et al. in patents (A to C) all teach to prepare HCV immunogenic composition by attaching the immunogenic protein/peptide(s) derived from non-structural protein NS4, NS5 and core to a particular immunogenic carrier of liposomes or ISCOM (See page 24 of A, column 10 in B and column 11 in C). ISCOM inherently comprises the active ingredients of saponin and cholesteritol. Both liposome and ISCOM are negatively charged antigen carriers/adjuvants by nature in light of the teaching by Sjolander et al. Moreover, none of references by Simmonds et al. or Sjolander et al. teach to use alum for conjugating the HCV antigen prior to contacting the HCV antigen to ISCOM complex. Simmond et al. do not teach the T cell epitopes of HCV antigen polyproteins.

24. Cerny et al. just teach there are many T cell epitopes in HCV antigen polypeptides core, NS3, NS4 and NS5, wherein 8 out or 9 CTL epitope listed in Table II are peptides positively charged. Therefore, the reference by Cerny et al. teaches the defect of the T cell epitope that is not taught by Simmond et al.

25. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references by Simmonds et al. in (A) or (B) or (C) and Cerny et al. to produce more significant T cell immune response using ISCOM to carried a HCV antigen that may contain one or more CTL epitopes. As there are no unexpected results have been provided, hence the claimed invention as a whole is *prima facie* obvious absence unexpected results.

26. **New ground rejection:**

Claim Rejections - 35 USC § 103

27. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

28. Claims 1, 44-45, 49-55, 63-66, 70-76 and 84-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garcon et al. (WO 96/33739A1) as applied to claims 1, 44-55, 64-66, 70-76, and further in view of Cerny et al. (J. Clin. Invest. 1995 Feb; 95(2):521-30) for claims 63 and 84-85.

29. Garcon et al. teach an immunogenic composition comprising an HCV antigen, and an organic complex comprising a saponin (QS21), cholestrosol that forms ISCOM structure, wherein the ISCOM is a negative charge adjuvant in nature. In contract to Applicants' assertion that Garcon's methodologies are related for encapsulation rather than electrostatically association, Carcon et al. cite on page 2 that "the antigen in the immunogenic complex can be contained within the vesicle membrane or contained outside the vesicle membrane. Preferably soluble antigens are **outside** and hydrophobic or lipidated antigen is either contained inside or outside the membrane. Carcon et al. also disclose that the vaccine composition formulated by ISCOM or other liposome will not require any specific carrier and be formulated in an aqueous or other pharmaceutically acceptable buffer. Whereas the alum or an oil in water emulsion is only an option rather than an obligation (See page 2). Further, Carcon et al. teach that liposome

may be aged into QS21/cholesterol mixture (ISCOM), which reduces the lytic activity of QS21 and increase the negative charge and stability of the complex of ISCOM (pages 6-8), wherein the liposome can be phospholipi, such as phospholipids A. Moreover, Carcon et al. also teach that the antigen composition formulated with ISCOM (SQ21+Sterol (SUV)) can be further added with MPL (QS21+SUV+MPL), such that the cytotoxic T cell activity is much higher than that comprising QS21 plus SUV or SQ21 alone. Garcon et al. do not teach the HCV antigen comprising at least 10 contiguous amino acid sequence defined as T cell epitope.

30. Cerny et al. teach HCV polyprotein antigens such as core, NS3, NS4and NS5 contain many T cell epitopes, and most of them listed in Table II are positively charged. Cerny et al. also describe a method for screening and testing those epitopes for the CTL activity.

31. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references by Carcon et al. and Cerny et al. to prepare an immunogenic composition using an ISCOM taught by Carcon et al. and HCV antigen comprising one or more CTL epitopes taught by Cerny et al. for producing an more significant T cell immune response. Hence the claimed invention as a whole is *prima facie* obvious absence unexpected results.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bao Qun Li/
Examiner, Art Unit 1648

